

Remarks

Claims 1, 3-5, 7-15, 17-22, 24, 34, 43, 56, and 76 were pending. Claims 3, 4, 22, and 76 were previously withdrawn from consideration. By this Amendment claims 1, 14, 15, 17, 18, 19, 20, 21, 24, 34, 43, and 56 are currently amended; claims 3-5, 12, 13, 22, and 76 are canceled without prejudice or disclaimer; and new claims 78-86 are added. No new matter is introduced.

New claims 78-82 correspond to original claims 38, 35, 37, 39, and 40, respectively.

New claims 83-86 correspond to original claims 48, 44, 45, and 47, respectively.

Prior Office Action

Applicant acknowledges withdrawal by the Examiner of all previous claim rejections under 35 U.S.C. §§ 112, first paragraph (written description).

Information Disclosure Statements

Applicant requests the Examiner to indicate he has considered references cited in Information Disclosure Statements originally received at the Patent Office on October 1, 2001, and September 30, 2002. Copies of these Information Disclosure Statements and the references cited therein were resubmitted with the previous response mailed January 26, 2004.

Applicant also requests the Examiner to indicate he has considered references cited in the Information Disclosure Statement originally filed on January 26, 2004 (received at the Patent Office January 28, 2004).

Claim Rejections Under 35 U.S.C. § 112, first paragraph (enablement)

The Examiner indicated (page 3 of the Office Action) that the specification is enabling for a method for:

(1) A method for inhibiting growth of a B-cell malignancy, wherein said B-cell malignancy is a marginal zone lymphoma or B-cell chronic lymphocytic leukemia (B-CLL), said method comprising administering to a subject having the B-cell malignancy:

(a) an immunostimulatory nucleic acid sequence that is 6 or more nucleotides in length and comprises an unmethylated CpG motif and a backbone modification, wherein said immunostimulatory nucleic acid is administered in an amount effective to upregulate expression of CD20, CD19, or CD22 in said B-cell malignancy; and

(b) an antibody chosen from an anti-CD20 antibody, an anti-CD19 antibody, and an anti-CD22 antibody,

wherein administration of the immunostimulatory nucleic acid and the antibody results in inhibition of growth of the B-cell malignancy;

(2) A method for reducing the growth of a B-cell malignancy, wherein said B-cell malignancy is B-CLL or marginal zone lymphoma, said method comprising isolating from a subject having said B-cell malignancy a B-CLL or marginal zone lymphoma cell, identifying a surface antigen chosen from CD19, CD20 and CD22, which is not expressed or which is expressed on the surface of the B-CLL or marginal zone lymphoma in an amount lower than that of a normal cell of the same type, and administering to said subject:

(a) an immunostimulatory nucleic acid sequence that is 6 or more nucleotides in length and comprises an unmethylated CpG motif and a backbone modification, wherein said immunostimulatory nucleic acid is administered in an amount effective to upregulate expression of CD20, CD19, or CD22 in said B-cell malignancy; and

(b) an antibody chosen from an anti-CD20 antibody, an anti-CD19 antibody, and an anti-CD22 antibody;

wherein the method results in reducing growth rate of the B-cell malignancy; and

(3) A method for reducing growth rate of a B-cell malignancy, wherein said B-cell malignancy is B-CLL or marginal zone lymphoma and wherein said B-CLL or said marginal zone lymphoma is resistant to antibody therapy, the method comprising administering to a subject having the B-cell malignancy:

(a) an immunostimulatory nucleic acid sequence that is 6 or more nucleotides in length and comprises an unmethylated CpG motif and a backbone modification, wherein said

immunostimulatory nucleic acid is administered in an amount effective to upregulate expression of CD20, CD19, or CD22 in said B-cell malignancy; and

(b) an antibody chosen from an anti-CD20 antibody, an anti-CD19 antibody, and an anti-CD22 antibody,

wherein the method results in reducing growth rate of the B-cell malignancy.

However, the Examiner rejected claims 1, 2 [sic], 5, 7-15, 17-21, 24, 34, and 43 under 35 U.S.C. § 112, first paragraph, as allegedly being not enabling for claims drawn to (1) preventing or completely curing B-cell malignancy in a subject, (2) inhibiting the growth of a B-cell malignancy other than B-CLL or marginal zone lymphoma, and (3) upregulating the expression of CD20, CD19, or CD22 in any cell other than a B-CLL or marginal zone lymphoma cell. For reasons set forth below, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection of claims 1, 5, 7-15, 17-21, 24, 34, and 43 under 35 U.S.C. § 112, first paragraph.

The Examiner appears to object, in part, to the notion of claims drawn to preventing or completely curing cancer in a subject. Applicant respectfully submits that current amendment of claims 1 and 24 to remove “subject at risk of developing a B-cell malignancy”, coupled with use of “treating” and/or “treat” as defined at page 32, lines 6-7 (reducing the symptoms of cancer, and/or inhibiting the growth of an established cancer), addresses the Examiner’s objection.

As noted above, the Examiner also asserts that the specification is not enabling for claims drawn to upregulating the expression of CD20, CD19, or CD22 in any cell other than a B-CLL or marginal zone lymphoma cell. In response, Applicant submits herewith a declaration by inventor George Weiner establishing that most B-cell malignancies other than plasmacytomas respond to CpG oligonucleotides (CpG ODN) by increasing expression of CD20. In particular, analysis of 41 individual patient-derived tumor samples revealed that B-cell chronic lymphocytic leukemia, small lymphocytic lymphoma, and marginal zone lymphoma were highly sensitive to CpG ODN, and follicular lymphoma, mantle cell lymphoma, and large cell lymphoma showed somewhat less but nevertheless substantial sensitivity to CpG ODN.

In view of this data, Applicant respectfully submits that, at least with respect to claims drawn to upregulation of the expression of CD20, such claims should not be limited only to B-CLL and marginal zone lymphoma because CpG upregulates CD20 in those as well as other types of B-cell malignancies, e.g., B-CLL, small lymphocytic lymphoma, marginal zone lymphoma, follicular lymphoma, mantle cell lymphoma, and large cell lymphoma.

Without meaning to concede the Examiner's assertion with respect to upregulation of CD19 and/or CD22, and solely for the purpose of advancing prosecution, claims 24, 34, and 43, drawn to methods involving an anti-CD19 antibody or an anti-CD22 antibody, are currently amended to specify that the B-cell malignancy is B-CLL or marginal zone lymphoma.

With respect to the Examiner's response at paragraph 8, page 11 of the Office Action, to Applicant's previous argument with respect to backbone modification, Applicant notes that the Examiner appears to have conceded that backbone modification need not be limited to phosphorothioate modification. Specifically, the Examiner states near the bottom of page 11 of the Office Action that "it is acknowledged that there are a number of well known backbone modifications which can be done to protect the oligonucleotide from nuclease degradation." In view of the foregoing, Applicant maintains the position that the claims are not limited to phosphorothioate oligonucleotides. For the record, Applicant respectfully disagrees with the Examiner's characterization of the previous argument as only an opinion because, at least with respect to nucleic acid delivery complexes, including, for example, nucleic acids encapsulated by liposomes, Applicant was trying to point out support within the specification for approaches for protecting against or overcoming degradation.

The foregoing notwithstanding, and solely for the purpose of advancing prosecution, claims 1, 24, 34, and 43 are currently amended to incorporate the limitation that the CpG oligonucleotide comprises a backbone modification.

Claims 5, 12, and 13 are canceled by this Amendment, rendering moot their rejection under 35 U.S.C. § 112, first paragraph.

For reasons provided above, Applicant submits that claims 1, 7-11, 14, 15, 17-21, 24, 34, and 43 are enabled. Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection of claims 1, 5, 7-15, 17-21, 24, 34, and 43 under 35 U.S.C. § 112, first paragraph.

Claim Rejections Under 35 U.S.C. § 103

Beginning at page 12 of the Office Action, the Examiner indicated that claims 1, 5, 7, 8, 9, 10, 12-14, 17-21, 24, 34, 43, and 56 are rejected as obvious over Wooldridge et al. (*Blood*, 1997; 89:2994-2998) in view of various additional references. For reasons provided below, Applicant respectfully disagrees and requests the Examiner to reconsider and withdraw the rejection of claims 1, 5, 7, 8, 9, 10, 12-14, 17-21, 24, 34, 43, and 56 under 35 U.S.C. § 103.

Claim 1 as currently amended is directed to a method for treating a B-cell malignancy, the method comprising: administering to a subject having a B-cell malignancy (a) an immunostimulatory CpG oligonucleotide between 6 and 100 nucleotides long comprising a backbone modification and at least the formula 5' X₁X₂CGX₃X₄ 3', wherein C is unmethylated and wherein X₁, X₂, X₃, and X₄ are nucleotides, in an effective amount to upregulate CD20 expression and (b) an anti-CD20 antibody, wherein the administering the CpG oligonucleotide and the anti-CD20 antibody results in treating the B-cell malignancy.

Wooldridge teaches that CpG oligonucleotide plus antibody specific for IgM idiotype, i.e., antibody specific for an antigen other than CD20, CD19, or CD22, induces increased killing of 38C13 lymphoma cells expressing the IgM idiotype compared to either CpG oligonucleotide alone or antibody alone. Wooldridge further teaches no direct effect of CpG oligonucleotide on tumor cells. Simply put, Wooldridge teaches that CpG oligonucleotide plus anti-X antibody increases killing of X-expressing cells compared to either CpG oligonucleotide alone or anti-X antibody alone.

The Examiner cites various references teaching that anti-Y antibody kills Y-expressing cells. The Examiner then attempts to combine these teachings with those of Wooldridge (CpG

oligonucleotide plus anti-X antibody increases killing of X-expressing cells compared to either CpG oligonucleotide alone or anti-X antibody alone). An attempt to make such combinations runs directly counter to a central tenet of biology, that antigen-specific antibodies have unique specificities and are not freely interchangeable. Therefore it is plain that, without more, there is no motivation to combine the teachings of Wooldridge (CpG oligonucleotide plus anti-X antibody increases killing of X-expressing cells compared to either CpG oligonucleotide alone or anti-X antibody alone) with a teaching that anti-Y antibody kills Y-expressing cells to arrive at a result (e.g., the claimed subject matter of claim 1) that CpG oligonucleotide plus anti-Y antibody increases expression of Y and killing of Y-expressing cells. Alternatively, it is also plain that, without more, there is no motivation to combine the teachings of Wooldridge (CpG oligonucleotide plus anti-X antibody increases killing of X-expressing cells compared to either CpG oligonucleotide alone or anti-X antibody alone) with a teaching that anti-Y antibody kills Y-expressing cells to arrive at a result (e.g., the claimed subject matter of claim 1) that CpG oligonucleotide plus anti-Y antibody increases expression of X and killing of X-expressing cells.

The Examiner expressly acknowledged that Wooldridge does not specifically indicate or teach that (1) oligonucleotide administration results in upregulation of CD20 expression (pages 13, 16, 18, and 20 of Office Action); (2) the method can utilize an anti-CD20 antibody (pages 14 and 16 of Office Action); (3) the anti-CD20 antibody used is specifically C2B8 (pages 14, 16, 19, and 22 of Office Action) or Rituximab (page 16 of Office Action); (4) the oligonucleotide and antibody can be administered together (pages 14, 16, 19, and 22 of Office Action); (5) the method can be used to treat marginal zone lymphoma cells using an anti-CD20 antibody (page 19 of Office Action); (6) the method can be used to [treat] B-cell lymphoma cells using an anti-CD20 antibody (page 22 of Office Action); (7) the oligonucleotide comprises an amino acid backbone modification (page 22 of Office Action); (8) the method can be used to treat B-cell lymphoma cells using an anti-CD19 or anti-CD22 antibody (page 24 of Office Action); or (9) the method can be used to treat cancer using an IgG1 isotype antibody (page 26 of Office Action).

Applicant wishes to point out to the Examiner that passages contained in Wooldridge provide a teaching away from the various proposed combinations. Specifically, Wooldridge

includes the following statement in the left-hand column on page 2997: “It is unlikely that the CpG ODN has a direct effect on tumor cells, given tumor proliferation was not inhibited in vitro by CpG ODN and only minimal therapeutic benefit was seen in the group treated with CpG ODN alone.” [Emphasis added] Wooldridge goes on to say in the right hand column on page 2997, “We detected no direct effect of the CpG ODN on 38C13 lymphoma cells ...” [Emphasis added] In contrast, the instant application teaches that CpG oligonucleotides are useful in combination with particular antibodies for the very reason that the CpG oligonucleotides have an effect on the tumor cells, namely, they induce expression on the tumor cells of antigens recognized by the antibodies. Thus in view of the teaching by Wooldridge that CpG oligonucleotide has no direct effect on tumor cells, e.g., upregulation of antigen expression on tumor cells, a person of skill in the art would understand there would be no reason to combine CpG oligonucleotide with any antibody or with any cell not disclosed in Wooldridge. Wooldridge goes on to speculate, in the right-hand column of page 2997, that “... it is possible the CpG ODN induced changes in the tumor cells that rendered them more sensitive to MoAb therapy. These studies therefore need to be confirmed in another tumor model and using other CpG ODN.” [Emphasis added] Needless to say, such speculation does not provide proper foundation for making an obviousness rejection because it cannot provide a reasonable expectation of success.

The Examiner repeatedly makes the assertion that malignant 38C13 lymphoma cells of Wooldridge are known to have a low level of CD20 expression. However, neither Wooldridge nor any art cited by the Examiner makes any teaching whatsoever as to the level of CD20 expression by 38C13 cells. Applicant therefore respectfully submits that the Examiner cannot rest an obviousness rejection on this unsupported assertion.

Turning now to specific rejections, the Examiner rejected claim 1 and claims 5, 7, 10, 12-14, and 17-21 (all dependent from claim 1) under 35 U.S.C. § 103(a) as being unpatentable over Wooldridge et al. (*supra*) in view of Taji et al. (*Japan J Cancer Res* July 1998; 89(7):748-756). According to the Examiner, Taji teaches that anti-CD20 antibodies (specifically, C2B8 antibodies), can be used to inhibit the growth of CD20-positive B-cell lymphoma cells

(specifically, SU-DHL-4 and SU-DHL-6 cells) which express low levels of CD20 (page 14 of Office Action). The Examiner asserts that it would have been prima facie obvious to administer to a subject having SU-DHL-4 or SU-DHL-6 the immunostimulatory CpG nucleic acid of Wooldridge with the C2B8 antibody taught by Taji. The Examiner alleged that motivation to make the combination is provided by Wooldridge, who teaches that when the oligonucleotide was used in combination with (a completely unrelated) antibody, it resulted in a synergistic effect. Applicant respectfully disagrees on the basis that the Examiner has failed to make a prima facie case for the obviousness rejection.

First, Applicant respectfully submits that Taji does not teach what the Examiner says it teaches. Contrary to the characterization by the Examiner, Taji teaches that anti-CD20 antibody C2B8 is useful only if CD20 is expressed at a level of at least 56.5×10^3 antibody binding sites per cell (Table I), i.e., at a high level. Taji found SU-DHL-4 and SU-DHL-6 were characterized as having 123.1×10^3 and 86.4×10^3 antibody binding sites per cell (Table I), as opposed to the CD20 weakly positive cell line NALL-1 (see abstract) with only 16.3×10^3 antibody binding sites per cell (Table I). The disclosure of Taji thus teaches that SU-DHL-4 and SU-DHL-6 cells express high levels, rather than low levels, of CD20.

Significantly, Wooldridge taken alone makes no teaching whatsoever as to the level of relevant surface antigen (IgM) expressed by 38C13 cells, including no teaching that CpG oligonucleotides have any effect on the level of surface IgM expression by 38C13 cells. Similarly, Wooldridge makes no teaching whatsoever as to the level of CD20 expressed by 38C13 cells, and, as acknowledged by the Examiner, no teaching that CpG oligonucleotides have any effect on the level of CD20 expression by 38C13 cells. In fact, there is no teaching or suggestion provided by Wooldridge that any surface antigen expressed by B-cell malignant cells can be upregulated by contact with CpG oligonucleotide.

Furthermore, with no teaching by Wooldridge that CpG oligonucleotide is effectively combined with any antibody other than the anti-idiotypic antibody there disclosed, there is no suggestion or motivation either to substitute the anti-CD20 antibody of Taji for the antibody of Wooldridge, or, conversely, to add CpG oligonucleotide of Wooldridge to the anti-CD20 antibody of Taji.

As noted above, there is no basis for making the suggested combination because to do so is tantamount to equating any one antibody (e.g., the antibody of Wooldridge, directed to an irrelevant antigen) with any other antibody (e.g., the anti-CD20 antibody of Taji), which is entirely contrary to the special feature of antigen-specificity that characterizes antibodies.

In view of the foregoing, it is clear that there is no suggestion or motivation to make the suggested combination and therefore the Examiner has failed to make a prima facie case for rejecting claim 1 and claims 5, 7, 10, 12-14, and 17-21 (all dependent from claim 1) under 35 U.S.C. § 103(a) as being unpatentable over Wooldridge in view of Taji et al. Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection.

The Examiner rejected claim 1 and claims 5, 7, 8, 10-14, and 17-21 (all dependent from claim 1) under 35 U.S.C. § 103(a) as being unpatentable over Wooldridge et al. (*supra*) in view of Winkler et al. (*Blood* 1999; 94(7):2217-2224). According to the Examiner, Winkler teaches that anti-CD20 antibodies (specifically, Rituximab, which is also referred to as “IDEC C2B8”) can be used to inhibit the growth of B-CLL lymphoma cells which express a low level of CD20. The Examiner asserts that it would have been prima facie obvious to administer to a subject having B-CLL lymphoma cells the immunostimulatory CpG nucleic acid of Wooldridge with the Rituximab antibody taught by Winkler. Similar to the rejection over Wooldridge in view of Taji, the Examiner alleged that motivation to make the combination is provided by Wooldridge, who teaches that when the oligonucleotide was used in combination with (an unrelated) antibody, it resulted in a synergistic effect. Applicant respectfully disagrees on the basis that the Examiner has failed to make a prima facie case for the obviousness rejection.

Contrary to the characterization by the Examiner, Winkler discloses only the number or percentage of CD20 positive cells in the population of B-CLL patients studied, rather than the level of expression of CD20 on individual B-CLL cells. For example, Table 1 of Winkler discloses that Patient No. 1 had 0.2×10^9 lymphocytes/L, of which 92.2 % were CD20 positive. In the absence of more information than provided by Winkler, it would be incorrect to equate a low number or percentage of CD20 positive cells with low expression of CD20 because, for example, all the CD20 positive cells might express CD20 very strongly.

Beginning at the bottom left hand column on page 2223, Winkler speculates as to CD20 expression on CLL cells, but Winkler offers no data to confirm or refute such speculation. Therefore Winkler provides no teaching as to the actual level of expression of CD20 on B-CLL cells.

As noted previously, Wooldridge makes no teaching whatsoever as to the level of CD20 expression by 38C13 cells, and Wooldridge does not specifically indicate or teach that oligonucleotide administration results in upregulation of CD20 expression. Without disclosure in Wooldridge or Winkler of the level of CD20 expression by 38C13 cells, or of upregulation of CD20 by CpG oligonucleotide, there is no suggestion or motivation to treat 38C13 cells with oligonucleotide and anti-CD20.

Furthermore, with no teaching by Wooldridge that CpG oligonucleotide is effectively combined with any antibody other than the anti-idiotypic antibody there disclosed, there is no suggestion or motivation either to substitute the anti-CD20 antibody of Winkler for the antibody of Wooldridge, or, conversely, to add CpG oligonucleotide of Wooldridge to the anti-CD20 antibody of Winkler.

As noted above, there is no basis for making the suggested combination because to do so is tantamount to equating any one antibody (e.g., the antibody of Wooldridge, directed to an irrelevant antigen) with any other antibody (e.g., the anti-CD20 antibody of Winkler), which is entirely contrary to the special feature of antigen-specificity that characterizes antibodies.

In view of the foregoing, it is clear that there is no suggestion or motivation to make the suggested combination and therefore the Examiner has failed to make a prima facie case for rejecting claim 1 and claims 5, 7, 8, 10-14, and 17-21 (all dependent from claim 1) under 35 U.S.C. § 103(a) as being unpatentable over Wooldridge in view of Winkler et al. Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection.

The Examiner rejected claim 1 and claims 5, 7, 9, 10, 12-14, and 17-21 (all dependent from claim 1) under 35 U.S.C. § 103(a) as being unpatentable over Wooldridge et al. (*supra*) in view of Taji et al. (*supra*) and further in view of Pawade et al. (*Histopathology* 1995; 27(2):129-137). The Examiner characterizes Pawade as teaching that marginal zone lymphoma cells are CD20 positive, indicating that marginal zone lymphoma cells express CD20 antigen. Applicant

respectfully disagrees on the basis that the Examiner has failed to make a prima facie case for the obviousness rejection.

Arguments presented above with respect to the rejection on the basis of Wooldridge and Taji also apply to this rejection, and they are not reproduced here for sake of brevity. As compared to the rejection on the basis of Wooldridge and Taji, the additional citation to Pawade adds only the observation that marginal zone lymphoma cells express CD20. The additional feature disclosed by Pawade does not remedy the previously noted deficiencies of the proposed combination of Wooldridge and Taji. Accordingly, there is no suggestion or motivation to make the suggested combination and therefore the Examiner has failed to make a prima facie case for rejecting claim 1 and claims 5, 7, 9, 10, 12-14, and 17-21 (all dependent from claim 1) under 35 U.S.C. § 103(a) as being unpatentable over Wooldridge in view of Taji et al. and further in view of Pawade et al. Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection.

The Examiner rejected claim 1 and claims 5, 7, 9, 10, 12-14, and 17-21 (all dependent from claim 1) under 35 U.S.C. § 103(a) as being unpatentable over Wooldridge et al. (*supra*) in view of Taji et al. (*supra*) and further in view of U.S. Pat. 5,969,135 (Ramasamy et al.). The Examiner characterizes Ramasamy as teaching that backbone modifications, including amino acid residue modification, can be made on therapeutic oligonucleotides in order to improve certain properties of the oligonucleotides, including increasing their stability towards enzymes. Applicant respectfully disagrees on the basis that the Examiner has failed to make a prima facie case for the obviousness rejection.

Arguments presented above with respect to the rejection on the basis of Wooldridge and Taji also apply to this rejection, and they are not reproduced here for sake of brevity. As compared to the rejection on the basis of Wooldridge and Taji, the additional citation to Ramasamy adds only the observation that the oligonucleotide can have a modified backbone. The additional feature disclosed by Ramasamy does not remedy the previously noted deficiencies of the proposed combination of Wooldridge and Taji. Accordingly, there is no suggestion or motivation to make the suggested combination and therefore the Examiner has failed to make a prima facie case for rejecting claim 1 and claims 5, 7, 9, 10, 12-14, and 17-21

(all dependent from claim 1) under 35 U.S.C. § 103(a) as being unpatentable over Wooldridge in view of Taji et al. and further in view of Ramasamy et al. Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection.

The Examiner rejected claims 24, 34, and 43 under 35 U.S.C. § 103(a) as being unpatentable over Wooldridge et al. (*supra*) in view of U.S. Pat. 6,306,393 (Goldenberg, filed May 10, 1999). The Examiner characterizes Goldenberg as teaching immunotherapy of B-cell malignancies using anti-CD22 antibodies, as well as anti-CD19 antibodies. Applicant respectfully disagrees on the basis that the Examiner has failed to make a prima facie case for the obviousness rejection.

Wooldridge offers no teaching whatsoever as to expression of CD19 or CD22 by 38C13 cells. There is no basis for making the suggested combination because to do so is tantamount to equating any one antibody (e.g., the antibody of Wooldridge, directed to an irrelevant antigen) with any other antibody (e.g., the anti-CD22 antibody or the anti-CD19 antibody of Goldenberg), which is entirely contrary to the special feature of antigen-specificity that characterizes antibodies.

Furthermore, with no teaching by Wooldridge that CpG oligonucleotide is effectively combined with any antibody other than the anti-idiotypic antibody there disclosed, there is no motivation either to substitute the anti-CD19 or anti-CD22 antibody of Goldenberg for the antibody of Wooldridge, or, conversely, to add CpG oligonucleotide of Wooldridge to the anti-CD19 or anti-CD22 antibody of Goldenberg.

Accordingly, it is clear that there is no suggestion or motivation to make the suggested combination and therefore the Examiner has failed to make a prima facie case for rejecting claims 24, 34, and 43 under 35 U.S.C. § 103(a) as being unpatentable over Wooldridge in view of Goldenberg. Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection.

The Examiner rejected Claim 56 under 35 U.S.C. § 103(a) as being unpatentable over Wooldridge et al. (*supra*) in view of U.S. Pat. 5,208,146 (Irie). According to the Examiner, Irie teaches a method of inhibiting the growth of tumors (such as human melanomas) by

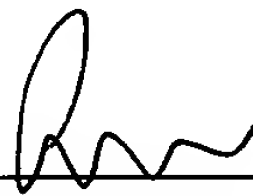
administering an IgG1 isotype antibody to a subject comprising a tumor that expresses an antigen recognized by the IgG1 isotype antibody. The Examiner asserts that it would have been prima facie obvious to administer to a subject having tumor cells the immunostimulatory nucleic acid taught by Woodridge and the IgG1 isotype antibodies taught by Irie to inhibit growth of the tumor cells. For reasons provided below, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection.

Claim 56 is currently amended to specify that the antibody is a human or humanized antibody of IgG1 isotype. Support for this amendment can be found in the specification, for example, at page 4, lines 5-9. By contrast, the IgG1 antibody disclosed in Irie is a murine IgG1 antibody. Applicant respectfully submits that it would not be obvious or even possible to combine the teachings of Wooldridge with the teachings of Irie to arrive at the subject matter claimed in claim 56 as currently amended because Irie teaches only a murine IgG1 antibody while claim 56 is directed to human or humanized antibody of IgG1 isotype. Therefore Applicant respectfully requests the Examiner to reconsider and withdraw the rejection of claim 56 under 35 U.S.C. § 103(a).

Summary

Claims 3-5, 12, 13, 22, and 76 are canceled. Claims 1, 14, 15, 17, 18, 19, 20, 21, 24, 34, 43, and 56 are currently amended. New claims 78-86 are added. Applicant requests indication of consideration by the Examiner of references cited in Information Disclosure Statements originally received by the Patent Office on October 1, 2001, September 30, 2002, and January 28, 2004. Applicant believes that claims 1, 7-11, 14, 15, 17-21, 24, 34, 43, 56, and 78-86 are in condition for allowance. An early and favorable response is earnestly solicited. The Examiner is invited to contact the undersigned by telephone to discuss any remaining issues of patentability.

Respectfully submitted,



Alan W. Steele Reg. No.: 45,128
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, MA 02210-2211
(617) 646-8000

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